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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/291,347	04/14/99	HANAK J	CACO-0051

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EXAMINER	
TUNG, P	
ART UNIT	**PAPER NUMBER**
1652	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/291,347	Applicant(s) Hanak et al.
	Examiner Peter Tung	Group Art Unit 1652

☒ Responsive to communication(s) filed on *Jan 5, 2001* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-18* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-5 and 7-18* is/are rejected.

☒ Claim(s) *6* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-18 and 36 are pending.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

3. Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, from which claims 3 and 36 depend upon already limits the cells producing the cellular component as the same cells producing RNase.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims are rejected under 35 U.S.C. 102(b) as being anticipated by Meador et al. With regard to claims 1-5, 9, 10, 11, 14-16, 18 and 36, Meador et al. teach (page 549-550, "Enzyme purification"; page 549, Abstract) a method comprising culturing cells constitutively expressing the non-specific RNase, RNase I, lysing said cells and purifying the cellular component RNase I. The cellular lysate comprises cellular components and RNase with sufficient activity to degrade all the RNA molecules present in the cell lysate. The instant claims are anticipated by Meador et al. as the bacteria are producing isolatable RNase I under cellular regulation (claim 11 and 14) and the RNase is secreted out of the cytoplasm and into the periplasm of the bacteria (claims 15 and 16).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 7, 8, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meador et al. as applied to claims 1 and 11, and further in view of Zhu et al. The teachings of Meador et al. have been discussed supra. Meador et al. do not teach purifying RNase I from a recombinant E. coli overproducing RNase I. With regard to claim 7, Zhu et al. teach (page 3147, "Results," 1st paragraph; Table 1) a method comprising culturing cells constitutively expressing recombinant *E. coli* RNase I and lysing said cells. The cellular lysate comprises cellular components and RNase with sufficient activity to degrade all the RNA molecules present in the cell lysate. With regard to claim 8, Zhu et al. also teach (page 3147, column 2, paragraphs 2 and 3; page 3148, Table 2) that DNA encoding RNase I is integrated into chromosomal DNA. With regard to claim 12, Zhu et al. also teach (page 3147, column 2, 2nd paragraph) that RNase I is overproduced by the cell. Zhu et al. do not teach isolating a cellular component from the cellular lysate. It would have been obvious to one of ordinary skill in the art at the time the invention was made to purify *E. coli* RNase I, as taught by Meador et al., from *E. coli* recombinantly expressing *E. coli* RNase I, as taught by Zhu et al., for the benefit of isolating large amounts of *E. coli* RNase I. One of ordinary

skill in the art is motivated to combine the two references as Zhu et al. teaches that purification of the RNase extracts is desirable so that RNase I can be separated from other RNase enzymes (page 3150, last paragraph). One of ordinary skill in the art would have a reasonable expectation of success at purifying RNase I as the teachings of Meador et al. show purifying *E. coli* RNase I and the teachings of Zhu et al. show expression of *E. coli* RNase I. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

9. Claims 13 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meador et al. as applied to claims 1, 11, 15 and 16, and further in view of Zhu et al and Clare et al. The teachings of Meador et al. have been discussed supra. Zhu et al. teach (page 3147, "Results," 1st paragraph; Table 1) a method comprising culturing cells constitutively expressing recombinant *E. coli* RNase I and lysing said cells. The cellular lysate comprises cellular components and RNase with sufficient activity to degrade all the RNA molecules present in the cell lysate. Zhu et al. further teach a plasmid comprising DNA encoding RNase I. Claims 13 and 17 add the further limitation of inducible production of RNase and secretion of the RNase in the medium, respectively. Meador et al. and Zhu et al. do not teach inducible production of RNase or secretion of RNase into the medium. Clare et al. teach (page 208, Table I) inducible production of protein in yeast where the yeast is secreted into the medium. Clare et al. teach (page 206-207, "Results and Discussion," part (a)) plasmids which allow secretion production of proteins in yeast. Protein production is under the control of an inducible promoter when this plasmid is integrated in the

appropriate yeast host. Clare et al. further teach (page 208, Table I) comparison of protein secreted into the medium and protein contained in the cells by lysis of yeast cells expressing heterologous protein. Clare et al. do not teach secretion production of RNase I or inducible production of RNase I. It would have been obvious to one of ordinary skill in the art at the time the invention was made to express and purify RNase I in yeast by secretion into the medium under inducible control and to lyse the cells for the benefits of secretion production of RNase I, inducible production of RNase I, and measurement of the amount of RNase I secreted into the medium. One of ordinary skill in the art is motivated to combine the references as Clare et al. teach (page 206, column 2, 2nd paragraph, lines 11-20) that the yeast secretion expression system is a general system which can be used for the secretion production of foreign proteins, Zhu et al. provide the teaching of DNA encoding RNase I and Meador et al. teach a method of purifying *E. coli* RNase I. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the inducible secretion expression of heterologous proteins in yeast is well known in the art and it would be a reasonable expectation to be able to express the RNase I, according to the teachings of Zhu et al., in the yeast system as taught by Clare et al. and to isolate the cellular component *E. coli* RNase I, according to the teachings of Meador et al. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

10. Applicants argue that Zhu et al. do not teach or suggest a method of preparing a substantially RNA-free cellular component and preparing a substantially RNA-free cellular

component. Applicants argue that there is no evidence in Zhu et al. that the RNase activity was sufficient to degrade substantially all of the RNA molecules in the lysate.

11. Applicant's arguments with respect to claims 1-5 amd 7-18 have been considered but are moot in view of the new ground(s) of rejection. As stated in the previous Office action, the cellular lysate comprises cellular components and RNase with sufficient activity to degrade all the RNA molecules present in the cell lysate. Applicants have not provided evidence to indicate that a bacterial cell producing RNase I would not have sufficient RNase activity to degrade substantially all the RNA molecules present in the cell lysate.

Allowable Subject Matter

12. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600